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Assistant Commissioner for Patents,  
Washington, D.C. 20231,  
On September 12, 2001

The Law Offices of Jonathan Alan Quine

By Tracie Brooks  
Tracie Brooks



Attorney Docket No. 02-020522US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Phillip A. Patten, *et al.*

Application No.: Not yet known

Filed:

For: METHODS AND COMPOSITIONS  
FOR POLYPEPTIDE ENGINEERING

Examiner: Unassigned

Art Unit: Unassigned

INFORMATION DISCLOSURE  
STATEMENT UNDER 37 CFR § 1.97 and  
§ 1.98

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

The references cited on attached PTO-1449 and 892 forms are being called to the attention of the Examiner to make of record references cited in parent application USSN 08/769,062 filed December 18, 1996. Pursuant to 37 CFR § 1.98(d), copies of references cited in parent application USSN 08/769,062 filed December 18, 1996 are not provided. Copy of 1449's from USSN 08/621,859 filed March 25, 1996 are included as well, as they were submitted in the parent application. However the applicants will gladly provided fresh copies of any references requested by the Examiner. It is respectfully requested that the cited

information on the previously submitted 1449 and 892 forms for application USSN 08/769,062 filed December 18, 1996 be expressly considered during the prosecution of this application, and that references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

Applicant believes that no fee is required for submission of this statement, since it is being submitted prior to the first Office Action. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 50-0893. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



Christopher C. Sappenfield  
Reg. No. 45,073

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Fax: (510) 337-7877

CCS: emg

<b>Substitute for form 1449A-B/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <b>COPY FROM PARENT</b> <i>(use as many sheets as necessary)</i>	<b>Complete if Known</b>	
	Application Number	<del>09/717419</del> <i>Unassigned</i>
	Filing Date	<del>November 18, 2000</del> <i>Unassigned</i>
	First Named Inventor	<b>Phillip A. Patten</b>
	Group Art Unit	<b>1634</b>
	Examiner Name	<b>S. Zitomer</b>
	Attorney Docket Number	<del>02-020520US</del> <i>02-020522US</i>

U.S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code (if known)			
	AA	5,427,930		Birkenmeyer et al.	06-27-1995	
	AB	5,792,607		Backman et al.	08-11-1998	

J1050 U.S. PTO  
09/954692  
09/12/01

FOREIGN PATENT DOCUMENTS								
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		Office	Number	Kind Code (if known)				

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T

Examiner Signature		Date Considered	
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	Application Number	<del>09/717449</del> <b>unassigned</b>
	Filing Date	<del>November 18, 2000</del> <b>unassigned</b>
	First Named Inventor	<b>Phillip A. Patten</b>
	Group Art Unit	<b>Unassigned</b>
	Examiner Name	<b>Unassigned</b>
Attorney Docket Number		<b>02-020520US 02-020522US</b>

U.S. PATENT DOCUMENTS						
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		Number	Kind Code (if known)			
	AA	6,096,548		Stemmer	08-01-2000	
	AB	6,117,679		Stemmer	09-12-2000	
	AC	6,132,970		Stemmer	10-17-2000	

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Examiner Initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
		Office	Number	Kind Code (if known)				
	AD	WO	98/42832		Cal Tech	10-01-1998		
	AE	WO	98/41653		Novo Nordisk	09-24-1998		
	AF	WO	99/29902		Cal Tech	06-17-1999		

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	AG	CARTER, "Improved Oligonucleotide-Directed Mutagenesis Using M13 Vectors," <u>Methods in Enzymology</u> , 154:382 (1987)		
	AH	KRAMER AND FRITZ, "Oligonucleotide-Directed Construction of Mutations via Gapped Duplex DNA," <u>Methods in Enzymology</u> , 154:350-367 (1987).		
	AI	KUNKEL, "Rapid and efficient site-specific mutagenesis without phenotypic selection," <u>PNAS</u> , 82:488-492 (Jan. 1985).		
	AJ	KUNKEL et al., "Rapid and Efficient Site-Specific Mutagenesis without Phenotypic Selection," <u>Methods in Enzymology</u> , 154:367-382 (1987).		
	AK	ZOLLER AND SMITH, "Oligonucleotide-Directed Mutagenesis: A Simple Method using Two Oligonucleotide Primers and a Single-Stranded DNA Template," <u>Methods in Enzymology</u> , 154:329 (1987).		
	AL	PRODROMOU et al., (1992) "Recursive PCR: a novel technique for total gene synthesis." <u>Protein Engineering</u> 5(8): 827-829.		
	AM	Statutory Declaration signed by Ruth Bird as filed in pending Australian opposition case, Australian Application No. 703264.		
	AN	Statutory Declaration signed by Ngaire Pettit-Young as filed in pending Australian opposition case, Australian Application No. 703264.		
	AO	Statutory Declaration signed by Mae Li Gan as filed in pending Australian opposition case, Australian Application No. 703264.		

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<p>Substitute for form 1449A-B/PTO</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p><b>COPY FROM PARENT</b> (use as many sheets as necessary)</p>	Complete if Known	
	Application Number	<del>00/717410</del> Unassigned
	Filing Date	<del>November 18, 2000</del> Unassigned
	First Named Inventor	Phillip A. Patten
	Group Art Unit	Unassigned
	Examiner Name	Unassigned
	Attorney Docket Number	<del>02-020520US</del> 02-020522US

AP	HIGUCHI et al., (1988) "A general method of <i>in vitro</i> preparation and specific mutagenesis of DNA fragments: study of protein and DNA interactions." <u>Nucleic Acids Research</u> 16(15): 7351-7367.	
AQ	SHI et al., (1993) "Rapid PCR Construction of a Gene Containing Lym-1 Antibody Variable Regions." <u>PCR Methods and Applications</u> 3: 46-53.	
AR	SHULDINER, A.R. et al., (1989) "Hybrid DNA artifact from PCR of closely related target sequences," <u>Nuc. Acids Res.</u> 17(11): 4409.	
AS	SANDHU, G.S. et al., (1992) "Dual Asymmetric PCR: One-Step Construction of Synthetic Genes," <u>Biotechniques</u> 12(01): 14-16.	
AT	Biotransformations, Pathogenesis, and Evolving Biotechnology, Program and Abstracts, <i>Pseudomonas '89</i> , American Society for Microbiology and The University of Illinois, July 9-13, 1989, Abstract Nos. 11-21 - 11-25, p. 26.	
AU	SMITH et al. (1991) "Localized sex in bacteria," <u>Nature</u> , 349: 29-31.	
AV	MICHAEL et al., (c. 1997) "Thermostable Ligase-Mediated Incorporation of Mutagenic Oligonucleotides During PCR Amplifications," <u>Methods in Molecular Biology</u> , Vol. 67, PCR Cloning Protocols: From Molecular Cloning to Genetic Engineering pp. 189-195.	
AW	NER et al. (1988) "Laboratory Methods: A Simple and Efficient Procedure for Generating Random Point Mutations and for Codon Replacements Using Mixed Oligodeoxynucleotides," <u>DNA</u> 7: 127-134.	
AX	MERYHANS et al., (1990) "DNA recombination during PCR," <u>Nuc Acids Res.</u> 18(7): 1687-1691.	
AY	WEBBER et al. (1983) "Formation of gene coding for hybrid proteins by recombination between related cloned genes in <i>E. coli</i> ." <u>Nuc. Acids Res.</u> 11(16): 5661-5669.	
AZ	POMPON et al. (1989) "Protein engineering by cDNA recombination in yeasts, shuffling of mammalian cytochrome P-450 functions." <u>Gene</u> 83: 15-24.	
BA	HORTON et al. (1990) "Gene splicing by overlap extension: Tailor-made genes using the polymerase chain reaction." <u>Biotechniques</u> 8(5): 528-535.	
BB	KLUG et al. (1991) "Creating chimeric molecules by PCR directed homologous DNA recombination." <u>Nuc. Acids Res.</u> 19(10): 2793.	
BC	ROUWENDAL et al., (1993) "Simultaneous Mutagenesis of Multiple Sites: Application of the Urase Chain Reaction Using PCR Products instead of Oligonucleotides." <u>Biotechniques</u> 15(1): 68-70, 72-74, 76.	

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Substitute for form 1449A-B/PTO  INFORMATION DISCLOSURE STATEMENT BY APPLICANT  <b>COPY FROM PARENT</b> <small>(a copy may be made for reference only)</small>	Complete if Known	
	Application Number	<del>08/05,002</del> Unassigned
	Filing Date	<del>December 18, 1996</del> Unassigned
	First Named Inventor	Phillip A. Patten
	Group Art Unit	1634
	Examiner Name	Zitomer, S.
	Attorney Docket Number	<del>02-020500US</del> 02-020522US

U.S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, lines, Where Relevant Passages or Relevant Figures Appeal
		Number	Kind Code (if known)			
	AA	4,766,106		Katre et al.	08-23-1988	
	AB	4,795,699		Tabor et al.	01-03-1989	
	AC	4,816,567		Cahilly et al.	03-28-1989	
	AD	4,902,502		Nitecki et al.	02-20-1990	
	AE	5,264,563		Huse	11-23-1993	
	AF	5,314,809		Erllich et al.	05-24-1994	
	AG	5,512,463		Stemmer	04-30-1996	
	AH	5,514,568		Stemmer	05-07-1996	
	AI	5,514,588		Varadaraj	05-07-1996	
	AJ	5,523,388		Huse	06-04-1996	
	AK	5,541,311		Dahlberg et al.	07-30-1996	
	AL	5,547,859		Goodman et al.	08-20-1996	
	AM	5,574,205		Kucherlapati et al.	11-12-1996	
	AN	5,667,974		Birkenmeyer et al.	09-16-1997	
	AO	5,698,426		Huse	12-16-1997	
	AP	5,756,316		Schellenberger	05-26-1998	
	AQ	5,770,434		Huse	06-23-1998	
	AR	5,808,022		Huse	09-15-1998	
	AS	5,824,496		Horwitz et al.	10-20-1998	
	AT	5,830,696		Short	11-03-1998	
	AU	5,843,643		Ratner	12-01-1998	
	AV	5,858,725		Crowe	01-12-1999	
	AW	5,866,363		Pieczenic	02-02-1999	
	AX	5,871,974		Huse	02-16-1999	
	AY	5,877,402		Maliga et al.	03-02-1999	
	AZ	5,885,813		Davis et al.	03-23-1999	
	BA	5,928,905		Stemmer et al.	07-27-1999	

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Substitute for form 1449A-B/PTO

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

Complete if Known

Application Number	<del>08/769,062</del> Unassigned
Filing Date	<del>December 18, 1996</del> Unassigned
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	02-020500US 02-020522US

**COPY FROM PARENT**  
(use as many sheets as necessary)

	BB	5,955,358		Huse	09-21-1999	
	BC	5,965,415		Radman et al.	10-12-1999	
	BD	6,001,574		Short	12-14-1999	
	BE	6,004,788		Short	12-21-1999	
	BF	6,015,694		Dubenskey et al.	01-18-2000	
	BG	6,000,710		Short	02-29-2000	
	BH	6,051,049		Hansen et al.	04-18-2000	
	BI	6,054,267		Short	04-25-2000	
	BJ	6,057,103		Short	05-02-2000	
	BK	6,071,889		Weiss et al.	06-06-2000	
	BL	6,074,853		Pati et al.	06-13-2000	
	BM	6,087,177		Wohlstadter	07-11-2000	
	BN	6,093,873		Chambon et al.	07-25-2000	
	BO	6,096,548		Stemmer	08-01-2000	
	BP	6,114,115		Wagner, Jr.	09-05-2000	
	BQ	6,117,679		Stemmer	09-12-2000	
	BR	6,132,970		Stemmer	10-17-2000	
	BS	6,153,410		Arnold et al.	11-28-2000	
	BT	6,159,687		Vind	12-12-2000	
	BU	6,171,820	B1	Short	01-09-2001	
	BV	6,174,673	B1	Short et al.	01-16-2001	
	BW	6,168,919	B1	Short	01-02-2001	
	BX	6,177,263	B1	Arnold et al.	01-23-2001	
	BY	5,795,747		Henco	08-18-1998	

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Examiner Initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
		Office	Number	Kind Code (if known)				
	BZ	EP	0 544 809	B1	lxsys, Inc.	12-16-1998		
	CA	EP	0 563 296	B1	lxsys, Inc.	03-17-1999		

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	Application Number	<del>08/769,062</del> Unassigned
	Filing Date	December 18, 1996 Unassigned
	First Named Inventor	Phillip A. Patten
	Group Art Unit	1634
	Examiner Name	Zitomer, S.
Attorney Docket Number		02-020500US 02-020522US

	CB	EP	0 552 266	B1	The Wellcome Foundation LTD.	01-19-2000		
	CC	EP	0 397 463	A2	Berlex Laboratories	11-14-1990		
	CD	EP	0 397 463	A3	Berlex Laboratories	11-14-1990		
	CE	WO	90/14424	A1	Scripps Clinic and Research Foundation	11-29-1990		
	CF	WO	92/06176	A1	IXSYS, Inc	04-16-1992		
	CG	WO	92/18645	A1	Henco	10-29-1992		
	CH	WO	93/01282	A1	Berlex Laboratories, Inc.	01-21-1993		
	CI	WO	93/18175	A1	Life Technologies, Inc.	09-16-1993		
	CJ	WO	93/19172	A1	Cambridge Antibody Technology LTD.	09-30-1993		
	CK	WO	94/11496	A1	IXSYS, Inc	05-26-1994		
	CL	WO	97/46670	A1	Massachusetts Institute of Technology	12-11-1997		
	CM	WO	99/29902	A1	California Institute of Technology	06-17-1999		

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T
	CN	ADEY ET AL. "Preparation of second-generation phage libraries." <i>Proteins</i> 227-291. (1996)	
	CO	Berger et al. "Prospective: Expanding the Potential of Restriction Endonucleases: Use of Hapaxotermistic Enzymes." <i>Anal Biochemistry</i> 222:1-8 (1994)	
	CP	Biotransformations <i>Amer Soc. Abstract</i> no.11-21&11-25 Pg.26 (July 1989)	
	CQ	CARTER "Improved Oligonucleotide-Directed Mutagenesis Using M13 Vectors." <i>Methods of Enzymology</i> 154:382-403 (1985)	
	CR	COLLET ET AL. "A binary plasmid system for shuffling combinational antibody libraries." <i>Proc. Natl. Acad. Sci. USA</i> 89(21):L10026-10030 (1992)	
	CS	DANGL ET AL. "Rapid Isolation of Cloned Isotype Switch Variants Using Fluorescent Activated Cell Sorting." <i>Cytometry</i> 2(6):395-401 (1982)	
	CT	DIERICK ET AL. "Incorporation of dITP of 7-deaza dGTP during PCR improves sequencing of the product." <i>Nuc. Acid Res.</i> 21(18):4427-4428 (1993)	
Examiner Signature	Date Considered		

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	First Named Inventor	<b>Phillip A. Patten</b>
	Group Art Unit	<b>1634</b>
	Examiner Name	<b>Zitomer, S.</b>
	Attorney Docket Number	<del>02-020500US</del> <b>02-020522US</b>

CU	FULLEN ET AL. "Genetic Algorithms and Recursive Ensemble Mutagenesis in Protein Engineering." <i>Complex.</i> Int. 94, from website (1992)	
CV	HEDA ET AL. "A simple in vitro site directed mutagenesis of concatamerized cDNA by inverse polymerase chain reaction." <i>Nuc. Acids Res.</i> 20(19):5241-5242 (1992)	
CW	HIGUCHI ET AL. "A general method of in vitro preparation and specific mutagenesis of DNA fragments study of protein and DNA interactions." <i>Nuc. Acids Res.</i> 16(15):7351-7367 (1988)	
CX	HODGSON "The Whys and Wherefores of DNA Amplification." <i>Biotechnology</i> 11(8):940-942 (1993)	
CY	Kang et al. "Antibody redesigned by chain shuffling from random combinatorial immunoglobulin libraries." <i>Proc. Natl. Acad. Sci. USA</i> 88(24):11120-11123 (1991)	
CZ	KLUG ET AL. "Creating chimeric molecules by PCR directed homologous DNA recombination." <i>Nuc Acids. Res.</i> 19(10):2793 (1991)	
DA	KOMANO ET AL. "Distribution of Shufflon among IncI Plasmids." <i>J. Bacteriology</i> 169(11):5317-5319. (1987)	
DB	KOMANO ET AL. "Physical and Genetic Analysis of IncI2 Plasmid R721: Evidence for the Presence of Shufflon." <i>Plasmid</i> 23:248-251. (1991)	
DC	KRAMER & FRITZ "Oligonucleotide-Directed Construction of Mutations via Gapped Duplex DNA." <i>Methods of Enzymology</i> 154:350-367 (1978)	
DD	Kunkel "Rapid and Efficient Site-Specific Mutagenesis without Phenotypic Selection." <i>Methods in Enzymology</i> 154:367-382 (1987)	
DE	KUNKEL "Rapid and efficient site-specific mutagenesis without phenotype selection." <i>Proc. Natl. Acad. Sci. USA</i> 82:488-492 (1985)	
DF	LOWNAM ET AL. "Affinity Maturation of Human Growth Hormone by Monovalent Phage Display." <i>J. Mol. Biol.</i> 234:654-678 (1993)	
DG	MAJUMDER "Ligation-free gene synthesis by PCR: synthesis and mutagenesis at multiple loci of a chimeric gene encoding OmpA signal peptide and hirudin." <i>Gene</i> 110(1):89-94 (1992)	
DH	MERYHANS ET AL. "DNA recombination during PCR." <i>Nuc Acids. Res.</i> 18(7):1687-1691 (1990)	
DI	MICHAEL "Thermostable Ligase-Mediated Incorporation of Mutagenic Oligonucleotides During PCR Amplification." <i>Meth. In Mol Biol.</i> 67:189-195 (1997)	
DJ	NER ET AL. "Laboratory Methods." <i>DNA</i> 7:127-134 (1988)	
DK	OLSEN ET AL. "Hybrid Baccillus (1-3,1-4)- $\beta$ -glucanases: engineering thermostable enzymes by construction of hybrid genes." <i>Mol. Gen. Genet</i> 225(2):177-185 (1987)	
DL	REIKOFSKI & TAO "Polymerase Chain Reaction (PCR) Techniques for Site-directed Mutagenesis." <i>Biotech Adv.</i> 10:535-547(1992)	
DM	ROBLES ET AL. "Hydropathy and Molar Volume Constraints on Combinatorial Mutants of the Photosynthetic Reaction Center." <i>J. Mol. Biol.</i> , 232:242-252 (1993)	
DN	ROUWENDAL ET AL. "Simultaneous Mutagenesis of Multiple Sites: Application of the Ligase Chain Reaction Using PCR Products Instead of Oligonucleotides." <i>Biotechniques</i> 15(1):68-70, 72-74, 76 (1993)	
DO	SANDHU ET AL. "Dual Asymmetric PCR: One-Step Construction of Synthetic Genes." <i>Biotechniques</i> 12(01):14-16 (1992)	

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	Group Art Unit	1634
	Examiner Name	Zitomer, S.
Attorney Docket Number		02-020500US-02-020522US

DP	SHI ET AL. "Rapid PCR Construction of a Gene Cotaining Lym-1 Antibody Variable Regions." <i>PCS Meth. &amp; Appl.</i> 3:46-52 (1993)	
DQ	SHULDINER ET AL. "Hybrid DNA artifact from PCR of closely related target sequences." <i>Nus. Acids Res.</i> 17(11):4409 (1989)	
DR	SMITH ET AL. "Localized sex in Bacteria." <i>Nature</i> 349:29-31 (1991)	
DS	Statutory Declaration by Mae Li Gan No. 703264	

DU	Statutory Declaration by Ruth Bird No. 703264	
DV	STEMMER ET AL. "A 20-Minute Ethidium Bromide High-slat Extraction Protocol for Pasmid DNA." <i>Biotechniques</i> 10(6):726 (1991)	
DW	STEMMER ET AL. "Enzymatic Inverse PCR- A Restriction Cite Independent, Single-Fragment Method for High-Efficiency, Site-Directed Mutagenesis." <i>Biotechniques</i> 13(2):214. (1992)	
DX	STEMMER ET AL. (1991) R342 "Expression of Antibody By Fragments Specific for a Heavy Metal Chelate (indium EDTA) in E-Coli." <i>J. Cell Biochem</i> 217	
DY	STEMMER ET AL. "Increased Antibody Expression for Escherichia-Coli Through Wobble-Base Library Mutagenesis by Enzymatic Inverse PCR." <i>Gene</i> 123(1):1-7. (1993)	
DZ	WU ET AL. "Allale-specific enzymatic amplification of $\beta$ -globin genomis DNA for diagnosis of sickle cell anema." <i>Proc. Natl. Acad. Sci</i> Vol 86:2757-2760. (1999)	
EA	ZOLLER & SMITH "Oligonucleotide-Directed Mutagenesis: A Simple Method using Two Oligonucleotide Primers and a Single-Stranded DNA Template." <i>Methods in Enzymology</i> 154:329-347 (1987)	

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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<b>Substitute for form 1449A-B/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <b>COPY FROM PARENT</b> <i>(use as many sheets as necessary)</i>	<b>Complete if Known</b>	
	Application Number	<del>08/769,082</del> <b>Unassigned</b>
	Filing Date	<del>December 18, 1996</del> <b>unassigned</b>
	First Named Inventor	<b>Phillip A. Patten</b>
	Group Art Unit	<b>1634</b>
	Examiner Name	<b>Zitomer, S.</b>
	Attorney Docket Number	<b>02-020500US-02-020522US</b>

U.S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code (if known)			
	AA	5,665,859		Wallach et al.	09-09-1997	
	AB	5,741,694		Hasrtup et al.	04-21-1998	
	AC	5,750,373		Garrard et al.	05-12-1998	
	AD	5,427,930		Birkenmeyer et al.	06-27-1995	
	AE	5,792,607		Backman et al.	08-11-1998	

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09/12/01

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		Office	Number	Kind Code (if known)				

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Approved for use through 10/31/99. OMB 0651-0031

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INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

Application Number ~~08/760,062~~ *unassigned*  
 Filing Date ~~December 18, 1996~~ *unassigned*  
 First Named Inventor **Phillip A. Patten**  
 Group Art Unit **1634**  
 Examiner Name **Zitomer, S.**  
 Attorney Docket Number ~~02-020500US~~ *02-020522US*

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		Number	Kind Code (if known)			
	AA	5,976,862		Kauffman et al.	11/02/1999	

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## FOREIGN PATENT DOCUMENTS

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INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

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Application Number 08/769,062 Unassigned  
 Filing Date December 18, 1996 Unassigned  
 First Named Inventor Phillip A. Patten  
 Group Art Unit 1634  
 Examiner Name Zitomer, S.  
 Attorney Docket Number 02-020500US-02-020522US

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		Number	Kind Code (if known)			
	AA	4,683,202		Mullis	07-28-1987	
	AB	4,800,159		Mullis et al.	01-24-1989	
	AC	4,965,188		Mullis et al.	10-23-1990	
	AD	5,023,171		Ho	06-11-1991	
	AE	5,176,995		Sninsky et al.	01-05-1993	
	AF	5,187,083		Mullis	02-16-1993	
	AG	5,234,824		Mullis	08-10-1993	
	AH	5,502,167		Waldmann	03-26-1996	
	AI	5,556,772		Sorge et al.	09-17-1996	
	AJ	5,714,316		Weiner et al.	02-03-1998	
	AK	5,851,813		Desrosiers	12-22-1998	
	AL	5,858,725		Crowe et al.	01-12-1999	

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		Office	Number	Kind Code (if known)				
	AM	WO	90/14430		Scripps Clinic & Research Found.	11-29-1990		
	AN	WO	91/06570		Univ. of Melbourne	05-16-1991		
	AO	WO	92/07075		Wellcome Foundation Ltd.	04-30-1992		
	AP	WO	93/02191		Wellcome Foundation Ltd.	02-04-1993		
	AQ	WO	93/06213		MRC	04-01-1993		
	AR	WO	93/11237		Wellcome Foundation Ltd.	06-10-1993		
	AS	WO	93/15208		Genzyme Ltd.	08-05-1993		
	AT	WO	93/16192		Wellcome Foundation Ltd.	08-19-1993		
Examiner Signature						Date Considered		

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Application Number	<del>00/769,062</del> <i>unassigned</i>
Filing Date	<del>December 18, 1996</del> <i>unassigned</i>
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	<del>02-020500US</del> <i>02-020522US</i>

AU	WO	93/18141	Biogen, Inc.	09-16-1993
AV	WO	93/25237	City of Hope	12-23-1993
AW	WO	94/03596	Univ. of Hawaii	02-17-1994
AX	WO	94/09817	City of Hope	05-11-1994
AY	WO	94/13804	Cambridge Antibody Tech. Ltd. Medical Res. Council	06-23-1994

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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	AZ	Delgrave et al., (1993) Bio/Technology <u>11</u> :1548-1552	
	BA	Goldman, E.R. and Youvan D.C., (1992) Bio/Technology <u>10</u> :1557-1561	
	BB	Joyce, G.F., (1992) Scientific American, December, 90-97	
	BC	Bock, L.C., et al., (1992) Nature <u>355</u> :564-566	
	BD	Scott, J.K. and Smith G.P., (1990) Science <u>249</u> :386-390	
	BE	Cwirla, S.E. et al., (1990) Proc Nat'l Acad Sci USA <u>87</u> :6378-6382	
	BF	McCafferty, J. et al., (1990) Nature <u>348</u> :552-554	
	BG	Cull, M.G. et al., (1992) Proc Natl Acad Sci USA <u>89</u> :1865-1869	
	BH	Nissim et al., (1994) ENBO J <u>13</u> :692-698	
	BI	Krishnan et al., (1991) Nucleic Acids Res. <u>19</u> (22):6177-6182	
	BJ	Klug et al., (1991) Nucleic Acids Res. <u>19</u> (10):2793	
	BK	Daugherty et al., (1991) Nucleic Acids Res. <u>19</u> :2471-2476	
	BL	Yolov et al. (1990) Nucleic Acids Res. <u>18</u> :3983-3986	
	BM	Jayaraman et al. (1991) Proc Natl Acad Sci USA <u>88</u> :4084-4088	
	BN	Morl, M and Schmelzer, C. (1990) Nucleic Acids Res. <u>18</u> (22):6545-6551	
	BO	Mullis et al., (1986) Cold Harbor Spring Symposia on Quantitative Biology <u>51</u> :263-273	
	BP	Sikorski et al., (1991) Methods in Enzymology <u>194</u> :302-318	
	BQ	Mullis et al., (1987) Methods in Enzymology <u>155</u> :335-350	

Examiner Signature		Date Considered	
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Application Number	<del>08/769,082</del> <i>unassigned</i>
Filing Date	<del>December 18, 1996</del> <i>unassigned</i>
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	<del>02-020500US</del> 02-020522US

BR	Scharf et al., (1986) Science <u>233</u> :1076-1078
BS	Saiki et al., (1988) Science <u>239</u> :487-491
BT	Saiki et al., (1986) Nature <u>324</u> (13):163-166
BU	Saiki et al., (1985) Science <u>230</u> :1350-1354
BV	Saiki et al., (1988) New Eng J Med <u>319</u> (9):537-541
BW	Crameri et al., (1993) Nucleic Acids Res. <u>21</u> (18):4410
BX	Villareal XC et al., (1991) Anal Biochem. <u>197</u> (2):362-367
BY	Jones et al., (1991) <i>Biotechniques</i> <u>10</u> (1):62-66
BZ	Weissenhorn et al., (1991) Gene <u>106</u> (2):273-277
CA	Majumder et al., (1992) Gene <u>110</u> (1):89-94
CB	Yao et al., (1992) PCR Methods Appl <u>1</u> (3):205-207
CC	Atreya et al (1992) Plant Mol Biol. <u>19</u> (3):517-522
CD	Zoller et al., (1992) Curr Opin Biotechnol. <u>3</u> (4):348-354
CE	Heda et al., (1992) Nucleic Acid Res. <u>20</u> (19):5241-5242
CF	Horton et al., (1993) Methods Enzymol <u>217</u> :270-279
CG	The whys and wherefores of DNA amplification. Biotechnology (NY). 1993 Aug; <u>11</u> (8):940-942
CH	Clackson et al., (1991) Nature <u>352</u> (6336):624-628
CI	Smith et al., (1993) PCR Methods Appl. <u>2</u> (3):253-257
CJ	Weisberg et al., (1993) <i>Biotechniques</i> <u>15</u> (1):68-70, 72-4, 76.
CK	Marks, et al., (1991) J Mol Biol <u>222</u> (3):581-597
CL	Harlow et al., (1994) Methods Mol Biol <u>31</u> :87-96
CM	Yon et al., (1989) Nucleic Acids Res. <u>17</u> (12):4895
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CO	Horton et al., (1990) <i>Biotechniques</i> <u>8</u> (5):528-535
CP	Osuna et al. (1991) Gene <u>106</u> :7-12
CQ	Dube et al. (1991) Biochemistry <u>30</u> (51):11760-7
CR	Ghosh et al., (1991) Biochem <u>30</u> :11767-74
CS	Paabo et al., (1990) J Biol Chem <u>265</u> (8):4718-4721

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	Application Number	<del>08/769,062</del> <b>unassigned</b>
	Filing Date	<del>December 18, 1996</del> <b>unassigned</b>
	First Named Inventor	<b>Phillip A. Patten</b>
	Group Art Unit	<b>1634</b>
	Examiner Name	<b>Zitomer, S.</b>
	Attorney Docket Number	<del>02-020500US</del> <b>02-020522US</b>

CT	Sambrook et al., (1989) Molecular cloning, A Laboratory Manual, 2 <sup>nd</sup> Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York.
CU	Opposition by Diversa Corporation filed in the matter of Australian Application 703264 Affymax Technology NV, September 23, 1999.

Examiner Signature		Date Considered	
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Application Number	<del>08/769,062</del> Unassigned
Filing Date	<del>December 18, 1996</del> Unassigned
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	<del>02-020500US</del> 02-020522US

## U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code (if known)			
	CV	5,958,672		Short	09-28-1999	
	CW	5,965,408		Short	10-12-1999	

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09/954692  
09/12/01

## FOREIGN PATENT DOCUMENTS

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## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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Application Number ~~08/769,002~~ *unassigned*  
 Filing Date ~~December 18, 1996~~ *unassigned*  
 First Named Inventor **Phillip A. Patten**  
 Group Art Unit **1634**  
 Examiner Name **Zitomer, S.**  
 Attorney Docket Number ~~02-020500US~~ *02-020522US*

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		Number	Kind Code (if known)				
	AA	5,939,250		Short	08/17/1999		

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09/954692  
09/12/01

## FOREIGN PATENT DOCUMENTS

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Application Number	<del>08/769,962</del> <i>unassigned</i>
Filing Date	<del>December 18, 1996</del> <i>unassigned</i>
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	<del>02-020500US</del> <i>02-020522US</i>

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Page 1 of 2

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Filing Date	<del>December 18, 1996</del> <i>unassigned</i>
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	<del>02-020500US</del> <i>02-020522US</i>


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<b>FORM PTO-1449 (Modified)</b> <b>LIST OF PATENTS AND PUBLICATIONS FOR</b> <b>APPLICANT'S INFORMATION DISCLOSURE</b> <b>STATEMENT (Use several sheets if necessary)</b>			Attorney Docket No.: 18097-02-025225 Applicant: Stemmer et al. Filing Date: March 25, 1996		Application No.: 08/621,855 Group: 1634 <i>unassigned</i>	
Reference Designation			U.S. PATENT DOCUMENTS			Page: 1
Examiner Initial	Document No.	Date	Name	Class	Sub-class	Filing Date (If Appropriate)
FOREIGN PATENT DOCUMENTS						
	Document No.	Date	Country	Class	Sub-class	Translate (Yes/No)
AA	WO 95/17413	6/29/95	PCT			
OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)						
EXAMINER			DATE CONSIDERED			

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 09/12/01



LIST OF PATENTS AND PUBLICATIONS FOR  
APPLICANT'S INFORMATION DISCLOSURE  
STATEMENT (Use several sheets if necessary)

Applicant: Stemmer et al.

unassigned

Filing Date: March 25, 1996

Group: 1634

## Reference Designation

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Page 1

Examiner Initial	Document No.	Date	Name	Class	Sub-class	Filing Date (IPAdm.)
AA	5,316,935	05/31/94	Arnold et al.			
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	Document No.	Date	Country	Class	Sub-class	
AD	WO 91/07506	05/30/91	PCT			
AE	WO 91/15581	10/17/91	PCT			
AF	WO 91/16427	10/31/91	PCT			
AG	WO 95/22625	08/24/95	PCT			
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AJ	Bartel et al., "Isolation of New Ribozymes From a Large Pool of Random Sequences", <u>Science</u> , 261:1411-1413 (1993)
AK	Cramer et al., "Combinatorial Multiple Cassette Mutagenesis Creates All The Permutations Of Mutant And Wild-Type Sequences", <u>Biotechniques</u> , 18(2):194-196 (1995)
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AM	Cramer et al., "Construction And Evolution Of Antibody-Phage Libraries By DNA Shuffling", <u>Nat. Med.</u> , 2(1):100-102 (1996) (previously submitted)
AN	Cramer et al., "Molecular Evolution Of An Arsenate Detoxification Pathway By DNA Shuffling", <u>Nat. Biotechnol.</u> , 15(5):436-438 (1997)
AO	Cramer et al., "DNA Shuffling Of A Family Of Genes From Diverse Species Accelerates Directed Evolution", <u>Nature</u> , 391(3664):288-291 (1998)
AP	Gates et al., "Affinity Selective Isolation Of Ligands From Peptide Libraries Through Display On A Lac Repressor 'Headpiece Dimer'", <u>J. Mol. Biol.</u> , 255(3):373-386 (1996) (previously submitted)
AQ	Gram et al., "In Vitro Selection and Affinity Maturation of Antibodies From a Naïve Combinatorial Immunoglobulin Library", <u>Proc. Natl. Acad. Sci. USA</u> , 89:3576-3580 (1992)
AR	Near, "Gene Conversion Of Immunoglobulin Variable Regions In Mutagenesis Cassettes By Replacement PCR Mutagenesis", <u>Biotechniques</u> , 12(1):88-97 (1992)
AS	Perlak, "Single Step Large Scale Site-Directed In Vitro Mutagenesis Using Multiple Oligonucleotides", <u>Nucleic Acids Res.</u> , 18(24):7457-7458 (1990)
AT	Stemmer, "Searching Sequence Space", <u>Biotechnology</u> , 13:549-553 (1995) (previously submitted)
AU	Stemmer et al., "Single-Step Assembly Of A Gene And Entire Plasmid From Large Numbers Of Oligodeoxyribonucleotides", <u>Gene</u> , 164(1):49-53 (1995) (previously submitted)
AV	Stemmer, "The Evolution of Molecular Computation", <u>Science</u> , 270(5241):1510 (1995) (previously submitted)
AW	Stemmer, "Sexual PCR and Assembly PCR" <u>Encyclopedia Mol. Biol.</u> , VCH Publishers, New York, pp. 447-457 (1996)
AX	Weber et al., "Formation of Genes Coding for Hybrid Proteins by Recombination Between Related, Cloned Genes in E. Coli," <u>Nucleic Acids Research</u> , 11(16):5661-5669 (1983)
AY	Weisberg et al., "Simultaneous Mutagenesis Of Multiple Sites: Application Of The Ligase Chain Reaction Using PCR Products Instead Of Oligonucleotides", <u>BioTechniques</u> , 15(1):68-76 (1993)

FORM PTO-1449 (Modified)

Attorney Docket No.: ~~1809-02-020220~~ Application No.: ~~08/621,819~~LIST OF PATENTS AND PUBLICATIONS FOR  
APPLICANT'S INFORMATION DISCLOSURE  
STATEMENT (Use several sheets if necessary)Applicant: Stemmer et al. *masque*

Filing Date: March 25, 1996

Group: 1634

<u>    </u> AZ	Zhang et al., "Directed Evolution Of A Fucosidase From A Galactosidase By DNA Shuffling And Screening", <i>Proc Natl. Acad. Sci. USA</i> , 94(9):4504-4509 (1997)
<u>    </u> BA	Zhao et al., "Molecular Evolution by Staggered Extension Process (StEP) In Vitro Recombination", <i>Nature Biotech.</i> , 16:258-261 (1998)

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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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<b>FORM PTO-1449 (Modified)</b> <b>LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)</b>			Attorney Docket No.: <u>02-020522US</u> Applicant: <u>Stemmer et al.</u> Filing Date: <u>March 25, 1996</u>		Application No.: <u>08/621,839</u> <u>unassigned</u> Group: <u>1634</u>	
<b>Reference Designation</b>			<b>U.S. PATENT DOCUMENTS</b>			Page 1
Examiner Initial	Document No.	Date	Name	Class	Sub-class	Filing Date (If Appropriate)
AA	5,830,721	11/03/98	Stemmer et al.			
AB	5,811,238	09/22/98	Stemmer et al.			
AC	5,763,192	06/09/98	Kauffman et al.			
AD	5,723,323	03/03/98	Kauffman et al.			
AE	5,814,476	09/29/98	Kauffman et al.			
AF	5,817,483	10/06/98	Kauffman et al.			
AG	5,824,514	10/20/98	Kauffman et al.			
AH						
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<b>FOREIGN PATENT DOCUMENTS</b>						
	Document No.	Date	Country	Class	Sub-class	Translation (Yes/No)
<b>OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>						
<b>EXAMINER</b>			<b>DATE CONSIDERED</b>			

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FORM PTO-1449 (Modified)

Attorney Docket

018097-014612US

Serial No.:

08/621,859

unassigned

LIST OF PATENTS AND PUBLICATIONS FOR  
APPLICANT'S INFORMATION DISCLOSURE  
STATEMENT

(Use several sheets if necessary)

Applicant: Stemmer and Crameri

Filing Date:

March 25, 1998 unassigned

Group:

3807

## Reference Designation

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Examiner Initial	Document No.	Date	Name	Class	Sub-class	Filing Date (If Appropriate)
___ AA	4,994,368	02/19/91	Goodman et al.			
___ AB	5,043,272	08/27/91	Hartley			
___ AC	5,093,257	03/03/92	Gray			
___ AD	5,223,408	06/29/93	Goeddel et al.			
___ AE	5,279,952	01/18/94	Wu			
___ AF	5,360,728	12/01/94	Prasher			
___ AG	5,521,077	05/28/96	Khosla et al			
___ AH	5,541,309	07/30/96	Prasher			
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___ AK	EP 252666 B1	01/13/88	Europe			
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___ AM	WO 91/01087	02/07/91	PCT			
___ AN	WO 95/17413	06/29/95	PCT			
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___ AP	Arkin et al., "An algorithm for protein engineering: Stimulation of recursive ensemble mutagenesis" <u>Proc. Natl. Acad. Sci. USA</u> 89:7811-7815 (1992).
___ AQ	Beaudry et al., "Directed evolution of an RNA enzyme" <u>Science</u> 257:635-641 (1992).
___ AR	Berger et al. "Phoenix mutagenesis: One-step reassembly of multiply cleaved plasmids with mixtures of mutant and wild-type fragments" <u>Anal. Biochem.</u> 214:571-579 (1993).

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FORM PTO-1449 (Modified)  LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		Attorney Docket <del>018097 014612US</del> <b>02-020522US</b>		Serial No.: <del>00/621,859</del> <b>Unassigned</b>	
		Applicant: Stemmer and Crameri		Filing Date: <b>Unassigned</b> <del>March 25, 1996</del>	
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Reference Designation (Including Author, Title, Date, Pertinent Pages, Etc.)					
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___ AS	Berkhout et al. "In vivo selection of randomly mutated retroviral genomes" <u>Nucleic Acids Res.</u> 21:5020-5023 (1993).				
___ AT	Cadwell et al. "Randomization of genes by PCR mutagenesis" <u>PCR Methods and Applications</u> 2:28-33 (1992). ( <i>previously submitted</i> )				
___ AU	Calogero et al. "In vivo recombination and the production of hybrid genes" <u>Microbiol. Lett.</u> 97:41-44 (1992).				
___ AV	Caren et al. "Efficient sampling of protein sequence space for multiple mutants" <u>Biotechnology</u> 12:517-520 (1994).				
___ AW	Delagrave et al. "Recursive ensemble mutagenesis" <u>Protein Engineering</u> 6:327-331 (1993).				
___ AX	Feinberg and Vogelstein "A technique for radiolabeling DNA restriction endonuclease fragments to high specific activity" <u>Anal. Biochem.</u> 132:6-13 (1983).				
___ AY	Heim et al. "Wavelength mutations and postranslational autoxidation of green fluorescent protein" <u>Proc. Natl. Acad. Sci. USA</u> 91:12501-12504 (1994).				
___ AZ	Hermes et al. "Searching sequence space by definably random mutagenesis: Improving the catalytic potency of an enzyme" <u>Proc. Natl. Acad. Sci. USA</u> 87:696-700 (1990).				
___ AAA	Ho et al. "Site-directed mutagenesis by overlap extension using the polymerase chain reaction" <u>Gene</u> 77:51-59 (1989).				
___ AAB	Horton et al. "Engineering hybrid genes without the use of restriction enzymes: Gene splicing by overlap extension" <u>Gene</u> 77:61-68 (1989).				
___ AAC	Jones et al. "Recombinant circle PCR and recombination PCR for site-specific mutagenesis without PCR product purification" <u>BioTechniques</u> 12:528-530, 532, 534-535 (1992).				
___ AAD	Kim et al. "Human immunodeficiency virus reverse transcriptase" <u>J. Biol. Chem.</u> 271:4872-4878 (1996).				
___ AAE	Leung et al. "A method for random mutagenesis of a defined DNA segment using a modified polymerase chain reaction" <u>Techniques</u> 1:11-15 (1989).				
EXAMINER			DATE CONSIDERED		

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<b>FORM PTO-1449 (Modified)</b>  <b>LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT</b> (Use several sheets if necessary)		Attorney Docket # <del>018097-014612US</del> <i>02-02052205</i>		Serial No.: <del>08/621,859</del> <i>Unassigned</i>	
Applicant: Stemmer and Cramer		Filing Date: <i>Unassigned</i> March 25, 1996		Group: 1807	
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Examiner Initial					
___ AAF	Marks et al. "By-passing immunization: Building high affinity human antibodies by chain shuffling" <u>Bio/Technology</u> 10:779-782 (1992).				
___ AAG	Meyerhans et al. "DNA recombination using PCR" <u>Nucleic Acids Res.</u> 18:1687-1691 (1990).				
___ AAH	Oliphant et al. "Cloning of random-sequence oligodeoxynucleotides" <u>Gene</u> 44:177-183 (1988).				
___ AAI	Pharmacia Catalog pp. 70-71 (1993 Edition).				
___ AAJ	Pompon et al. "Protein engineering by cDNA recombination in yeasts: Shuffling of mammalian cytochrome P-450 functions" <u>Gene</u> 83:15-24 (1989).				
___ AAK	Reidhaar-Olson et al. "Combinatorial cassette mutagenesis as a probe of the informational content of protein sequences" <u>Science</u> 241:53-57 (1988).				
___ AAL	Rao et al. "Recombination and polymerase error facilitate restoration of infectivity in brome mosaic virus" <u>J. Virol.</u> 67:969-979 (1993).				
___ AAM	Stemmer et al. "Selection of an active single chain Fv antibody from a protein linker library prepared by enzymatic inverse PCR" <u>BioTechniques</u> 14:256-265 (1992).				
___ AAN	Stemmer et al. "Rapid evolution of a protein in vitro by DNA shuffling" <u>Nature</u> 370:389-391 (1994). <i>(previously submitted)</i>				
___ AAO	Stemmer et al. "DNA shuffling by random fragmentation and reassembly: In vitro recombination for molecular evolution" <u>Proc. Natl. Acad. Sci. USA</u> 91:10747-10751 (1994). <i>(previously submitted)</i>				
EXAMINER		DATE CONSIDERED			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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FORM PTO-1449 (Modified)

Attorney Docket No.

Serial No.:

~~18097-020500~~ 02-020522US 08/769,062 *unassigned*LIST OF PATENTS AND PUBLICATIONS FOR  
APPLICANT'S INFORMATION DISCLOSURE  
STATEMENT

(Use several sheets if necessary)

Applicant: PHILLIP A. PATTEN et al.

Filing Date: ~~12/18/96~~  
*unassigned*

Group: Unknown

## Reference Designation

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Examiner Initial	Document No.	Date	Name	Class	Sub-class	Filing Date (If Appropriate)
___ AA	3,817,837	06/18/74	Rubenstein et al.	195		
___ AB	3,850,752	11/26/74	Schuurs et al.	G01N 31	14	
___ AC	3,939,350	02/17/76	Kronick et al.	G01T 1	20	
___ AD	3,996,345	12/07/76	Ullman et al.	G01N 21	00	
___ AE	4,275,149	06/23/81	Litman et al.	B12Q 1	66	
___ AF	4,277,437	07/07/81	Maggio	G01N 33	54	
___ AG	4,366,241	12/28/82	Tom et al.	G01N 33	54	
___ AH						
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___ AK						
___ AL						

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___ AM	WO 94/12305	06/09/94	PCT	B23B 51	00	Yes
___ AN	WO 95/11995	05/04/95	PCT	C12Q 1	68	No
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___ AP						
___ AQ						

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___ AR	An, S. et al., "Cloning, sequencing and tissue distribution of two related G protein-coupled receptor candidates expressed prominently in human lung tissue," <u>FEBS Letts.</u> 375:121-124 (1995)
___ AS	Andersson D.I. et al., "Muller's ratchet decreases fitness of a DNA-based microbe," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 93:906-907 (1996)
___ AT	Barak, L.S. et al., "The Conserved Seven-Transmembrane Sequence NP(X) <sub>2</sub> Y of the G-Protein-Coupled Receptor Superfamily Regulates Multiple Properties of the $\beta_2$ -Adrenergic Receptor," <u>Biochemistry</u> 34:15407-15414 (1995)
___ AU	Barnes, W.M., "PCR amplification of up to 35-kb DNA with high fidelity and high yield from $\lambda$ bacteriophage templates," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 91:2216-2220 (1994)
___ AV	Barry, M.A. et al., "Toward cell-targeting gene therapy vectors: Selection of cell-binding peptides from random peptide-presenting phage libraries," <u>Nature Med.</u> 2(3):299-305 (1996)

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LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		Applicant: PHILLIP A. PATTEN et al.	
		Filing Date: <i>12/18/96</i> <b>unassigned</b>	Group: Unknown

  

___ AW	Benka, M.L. et al., "The thrombin receptor in human platelets is coupled to GTP binding protein of the $G\alpha_q$ family," <u>FEBS Letts.</u> 363:49-52 (1995)
___ AX	Berek, C. et al., "Mutation Drift and Repertoire Shift in the Maturation of Immune Response," <u>Immunological Reviews</u> 96:23-41 (1987)
___ AY	Bird, R.E. et al., "Single-Chain Antigen-Binding Proteins," <u>Science</u> 242:423-426 (1988)
___ AZ	Broach, J.R. et al., "High-throughput screening for drug discovery," <u>Nature Supp.</u> 384:14-16 (1996)
___ BA	Cadwell, R.C. et al., "Randomization of Genes by PCR Mutagenesis," <u>PCR Methods and Applications</u> 2:28-33 (1992)
___ BB	Cantwell, C.A. et al., "Cloning and expression of a hybrid <i>Streptomyces clavuligerus</i> cef E gene in <i>Penicillium chrysogenum</i> ," <u>Curr. Genet.</u> 17:213-221 (1990)
___ BC	Chen, C.C.H. et al., "Structure of a Phosphonate-inhibited $\beta$ -Lactamase, An Analog of the Tetrahedral Transition State/Intermediate of $\beta$ -Lactam Hydrolysis," <u>J. Mol. Biol.</u> 234:165-178 (1993)
___ BD	Chen, K. et al., "Tuning the activity of an enzyme for unusual environments; Sequential random mutagenesis of subtilisin E for catalysis in dimethylformamide," <u>Proc. Natl. Acad. Sci. U.S.A.</u> , 90:5618-5622 (1993)
___ BE	Chong, S. et al., "Protein Splicing Involving the <i>Saccharomyces cerevisiae</i> VMA Intein," <u>J. Biol. Chem.</u> 271(36):22159-22168 (1996)
___ BF	Courtney, L.P. et al., "An anti-IL-2 antibody increases serum half-life and improves anti-tumor efficacy of human recombinant interleukin-2," <u>Immunopharmacology</u> 28:223-232 (1994)
___ BG	Cramer, A. et al., "Construction and evolution of antibody-phage libraries by DNA shuffling," <u>Nature Medicine</u> 2(1):100-102 (1996)
___ BH	Cramer, A. et al., "Improved Green Fluorescent Protein by Molecular Evolution Using DNA Shuffling," <u>Nature Biotech.</u> 14:315-319 (1996)
___ BI	Dangl, J.L. et al., "Rapid Isolation of Cloned Isotype Switch variants Using Fluorescence Activated Cell Sorting," <u>Cytometry</u> 2(6):395-401 (1982)
___ BJ	Dierick, H. et al., "Incorporation of DITP or 7-deaza dGTP during PCR improves sequencing of the product," <u>Nucl. Acids Res.</u> 21(18):4427-4428 (1993)
___ BK	Duncan, R. et al., "Polymer Conjugates, Pharmacokinetic Considerations for Design and Development," <u>Clin. Pharmacokinet.</u> 27(4):290-306 (1994)
___ BL	Dunn, I.S., "Assembly of Functional Bacteriophage Lambda Virions Incorporating C-Terminal Peptide or Protein Fusions with the Major Tail Protein," <u>J. Mol. Biol.</u> 248:497-506 (1995)
___ BM	Fish, E.N. et al., "Human Leukocyte Interferon Subtypes have Different Antiproliferative and Antiviral Activities on Human Cells," <u>Biochem. Biophys. Res. Commun.</u> 112(2):537-546 (1983)
___ BN	Gascoigne, N.R.J. et al., "Secretion of a chimeric T-cell receptor-immunoglobulin protein," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 84:2936-2940 (1987)
___ BO	Gates, C.M. et al., "Affinity Selective Isolation of Ligands from Peptide Libraries Through Display on a lac Repressor 'Headpiece Dimer'" <u>J. Mol. Biol.</u> 255:373-386 (1996)

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LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		Applicant: PHILLIP A. PATTEN et al.	
		Filing Date: <b>unassigned</b> <del>12/18/96</del>	Group: Unknown
___ BP	Gram, H. et al., "Phage display as a rapid gene expression system: production of bioactive cytokine-phage and generation of neutralizing monoclonal antibodies," <u>J. Immunological Methods</u> 161:169-176 (1993)		
___ BQ	Hartl, F.U., "Molecular chaperones in cellular protein folding," <u>Nature</u> 381:571-580 (1996)		
___ BR	Higazi, A.A et al., "Single-Chain Urokinase-Type Plasminogen Activator Bound to its Receptor is Relatively Resistant to Plasminogen Activator Inhibitor Type 1," <u>Blood</u> 87(9):3545-3549 (1996)		
___ BS	Hogan, J.C., "Directed combinatorial chemistry," <u>Nature Supp.</u> 384:17-19 (1996)		
___ BT	Holskin, B.P. et al., "A Continuous Fluorescence-Based Assay of Human Cytomegalovirus Protease Using a Peptide Substrate," <u>Anal. Biochem.</u> 226:148-155 (1995)		
___ BU	Horisberger, M.A. et al., "Interferon-Alpha Hybrids," <u>Pharmac. Ther.</u> 66(3):507-534 (1995)		
___ BV	Hu, R. et al., "Evidence for Multiple Binding Sites for Several Components of Human Lymphoblastoid Interferon- $\alpha$ ," <u>J. Biol. Chem.</u> 268(17):12591-12595 (1993)		
___ BW	Janda, K.D. et al., "Direct selection for a catalytic mechanism from combinatorial antibody libraries," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 91:2532-2536 (1994)		
___ BX	Kang, Y.S. et al., "Effects of Expression of Mammalian G $\alpha$ and Hybrid Mammalian-Yeast G $\alpha$ Proteins on the Yeast Pheromone Response Signal Transduction Pathway," <u>Mol. Cell Biol.</u> 10(6):2582-2590 (1990)		
___ BY	Khosla, C. et al., "Generation of polyketide libraries via combinatorial biosynthesis," <u>TIBTECH</u> 14 (1996)		
___ BZ	Kim, B. et al., "Human immunodeficiency virus reverse transcriptase substitutes for DNA polymerase I in <i>Escherichia coli</i> ," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 92:684-688 (1995)		
___ CA	Kirpekar, F. et al., "7-Deaza Purine Bases Offer a Higher Ion Stability in the Analysis of DNA by Matrix-assisted Laser Desorption/Ionization Mass Spectrometry," <u>Rapid Communications in Mass Spectrometry</u> 9:525-531 (1995)		
___ CB	Kontsek, P., "Human Type I Interferons: Structure and Function," <u>Acta Virologica</u> 38:345-360 (1994)		
___ CC	Kristensen, C. et al., "A single-chain insulin-like growth factor I/insulin hybrid binds with high affinity to the insulin receptor," <u>Biochem. J.</u> 305:981-986 (1995)		
___ CD	Langer, J.A. et al., "Binding of Human Alpha-Interferons to Natural Killer Cells," <u>J. Interferon Res.</u> 6:97-105 (1986)		
___ CE	Lathrop, R.H. et al., "Global Optimum Protein Threading with Gapped Alignment and Empirical Pair Score Functions," <u>J. Mol. Biol.</u> 255:641-665 (1996)		
___ CF	Levichkin, I.V. et al., "A New Approach to Construction of Hybrid Genes: Homolog Recombination Method," <u>Mol. Biol.</u> 29(5):572-577 (1995)		
___ CG	Li, J. et al., "Single Chain Human Interleukin 5 and Its Asymmetric Mutagenesis for Mapping Receptor Binding Sites," <u>J. Biol. Chem.</u> 271(4):1817-1820 (1996)		
___ CH	Lotze, M.T. et al., "High-Dose Recombinant Interleukin 2 in the Treatment of Patients with Disseminated Cancer," <u>J. Amer. Med. Assoc.</u> 256(22):3117-3124 (1986)		

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LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		Applicant: PHILLIP A. PATTEN et al.	
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___ CI	Lundberg, K.S. et al., "High-fidelity amplification using a thermostable DNA polymerase isolated from <i>Pyrococcus furiosus</i> ," <u>Gene</u> 108:1-6 (1991)
___ CJ	Mattheakis, L. C. et al., "As in vitro polysome display system for identifying ligands from very large peptide libraries," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 91:9022-9026 (1994)
___ CK	Matthews, D.J. et al., "Substrate Phage: Selection of Protease Substrates by Monovalent Phage Display," <u>Science</u> 260:1113-1117 (1993)
___ CL	McCafferty, J. et al., "Selection and Rapid Purification of Murine Antibody Fragments That Bind a Transition-State Analog by Phage Display," <u>Applied Biochem. Biotech.</u> 47:157-173 (1994)
___ CM	Medberry, S.L. et al., "Intra-chromosomal rearrangements generated by Cre-lox site-specific recombination," <u>Nucl. Acids Res.</u> 23(3):485-490 (1995)
___ CN	Meister, A. et al., "Biological Activities and Receptor Binding of Two Human Recombinant Interferons and their Hybrids," <u>J. Gen. Virol.</u> 67:1633-1643 (1986)
___ CO	Metcalf, W.W. et al., "Mutational Analysis of an <i>Escherichia coli</i> Fourteen-Gene Operon for Phosphonate Degradation, Using Tnp <sup>hoA</sup> Elements," <u>J. Bacteriology</u> 175(11):3430-3442 (1993)
___ CP	Northrup, J.P. et al., "Characterization of the Nuclear and Cytoplasmic Components of the Lymphoid-specific a Nuclear Factor of Activated T Cells (NF-AT) Complex," <u>J. Biol. Chem.</u> 268(4):2917-2923 (1993)
___ CQ	Nürnberg, B. et al., "Receptors and G proteins as primary components of transmembrane signal transduction," <u>J. Mol. Med.</u> 73:123-132 (1995)
___ CR	Ohnishi, H. et al., "Prolongation of Serum Half-Life of Interleukin 2 and Augmentation of Lymphokine-activated Killer Cell Activity by Pepstatin in Mice," <u>Canc. Res.</u> 50:1107-1112 (1990)
___ CS	O'Neil, K.T. et al., "Phage display: protein engineering by directed evolution," <u>Curr. Op. Struct. Biol.</u> 5:443-449 (1995)
___ CT	Ortaldo, J.R. et al., "A species of human $\alpha$ interferon that lacks the ability to boost human natural killer activity," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 81:4926-4929 (1984)
___ CU	Overall, M.L. et al., "Different Interactions of Interferon- $\alpha$ Subtypes at the Surface of Epithelial and Lymphoid Cells," <u>J. Interferon Res.</u> 12:281-288 (1992)
___ CV	Ozes, O.N. et al., "A Comparison of Interferon-Con1 with Natural Recombinant Interferons- $\alpha$ : Antiviral, Antiproliferative, and Natural Killer-Inducing Activities," <u>J. Interferon Res.</u> 12:55-59 (1992)
___ CW	Panka, D.J. et al., "Variable region framework differences result in decreased or increased affinity of variant anti-digoxin antibodies," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 85:3080-3084 (1988)
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___ CY	Parker, L.T. et al., "Peak Height Variations in Automated Sequencing of PCR Products Using Taq Dye-Terminator Chemistry," <u>BioTechniques</u> 19(1):116-121 (1995)
___ CZ	Patten, P.A. et al., "The Immunological Evolution of Catalysis," <u>Science</u> 271:1086-1091 (1996)



LIST OF PATENTS AND PUBLICATIONS FOR  
APPLICANT'S INFORMATION DISCLOSURE  
STATEMENT

(Use several sheets if necessary)

~~18097-020500~~~~08/769,062~~

Applicant: PHILLIP A. PATTEN et al.

Filing Date: ~~12/18/96~~

Group: Unknown

___ DA	Pérez-Pérez, J. et al., "Increasing the Efficiency of Protein Export in <i>Escherichia coli</i> ," <u>Biotechnology</u> 12:178-180 (1994)
___ DB	Pérez-Pérez, J. et al., "DNAK/DNAJ Supplementation Improves the Periplasmic Production of Human Granulocyte-Colony Stimulating Factor in <i>Escherichia coli</i> ," <u>Biochem. Biophys. Res. Commun.</u> 210(2):524-529 (1995)
___ DC	Post, G.R. et al., "G protein-coupled receptors and signaling pathways regulating growth responses," <u>FASEB J.</u> 10:741-749 (1996)
___ DD	Price, L.A. et al., "Functional Coupling of a Mammalian Somatostatin Receptor to the Yeast Pheromone Response Pathway," <u>Mol. Cell Biol.</u> 15(11):6188-6195 (1995)
___ DE	Pugsley, A.P., "The Complete General Secretory Pathway in Gram-Negative Bacteria," <u>Microbiol. Rev.</u> 57(1):50-108 (1993)
___ DF	Ranu, R.S., "DNA Sequencing with $\Delta$ Taq <sup>®</sup> DNA Polymerase," <u>BioTechniques</u> 18(3):390-395 (1995)
___ DG	Raport, C.J. et al., "The orphan G-protein-coupled receptor-encoding gene <i>V28</i> is closely related to genes for chemokine receptors and is expressed in lymphoid and neural tissues," <u>Gene</u> 163:295-299 (1995)
___ DH	Rashtchian, A., "Novel methods for cloning and engineering genes using the polymerase chain reaction," <u>Current Op Biotech.</u> 6:30-36 (1995)
___ DI	Reisine, T. et al., "Molecular Mechanisms of Opiate Receptor Coupling to G Proteins and Effector Systems," <u>Annals N.Y. Acad. Sci.</u> 780:168-175 (1996)
___ DJ	Rohlmann, A. et al., "Sustained somatic gene inactivation by viral transfer of Cre recombinase," <u>Nature Biotechnology</u> 14:1562-1565 (1996)
___ DK	Rosenberg, A.H. et al., "Effects of Consecutive AGG Codons on Translation in <i>Escherichia coli</i> , Demonstrated with a Versatile Codon Test System," <u>J. Bacteriology</u> 175(3):716-722 (1993)
___ DL	Saggio, I. et al., "Functional phage display of ciliary neurotrophic factor," <u>Gene</u> 152:35-39 (1995)
___ DM	Sandkvist, M. et al., "Secretion of recombinant proteins by Gram-negative bacteria," <u>Current Op. Biotech.</u> 7:505-511 (1996)
___ DN	Sauer, B. et al., "Site-specific DNA recombination in mammalian cells by the Cre recombinase of bacteriophage P1," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 85:5166-5170 (1988)
___ DO	Schatz, P.J. et al., "Genetic Analysis of Protein Export in <i>Escherichia coli</i> ," <u>Ann. Rev. Genet.</u> 24:215-248 (1990)
___ DP	Scheidl, T.M. et al., "Automated Fluorescent Dye-Terminator Sequencing of G+C-Rich Tracts with the Aid of Dimethyl Sulfoxide," <u>Biotechniques</u> 19:691-694 (1995)
___ DQ	Seed, B. et al., "Molecular cloning of the CD2 antigen, the T-cell erythrocyte receptor, by a rapid immunoselection procedure," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 84:3365-3369 (1987)
___ DR	Seed, B., "Developments in expression cloning," <u>Current Op. Biotech.</u> 6:567-573 (1995)
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___ DT	Shenker, A., "G Protein-coupled receptor structure and function: the impact of disease-causing mutations," <u>Baillieres Clin. Endo. Metab.</u> 9(3):427-451 (1995)

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LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		Applicant: PHILLIP A. PATTEN et al.	
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___ DU	Siderovski, D.P. et al., "A new family of regulators of G-protein-coupled receptors?" <u>Current Biology</u> 6(2):211-212 (1996)		
___ DV	Simonen, M. et al., "Protein Secretion in <i>Bacillus</i> Species," <u>Microbiol. Rev.</u> 57(1):109-137 (1993)		
___ DW	Skatrud, P.L. et al., "Genetic engineering of $\beta$ -lactam antibiotic biosynthetic pathways in filamentous fungi," <u>TIBTECH</u> 10:324-329 (1992)		
___ DX	Skerra, A. et al., "Filter Screening of Antibody Fab Fragments Secreted from Individual Bacterial Colonies: Specific Detection of Antigen Binding with a Two-Membrane System," <u>Anal. Biochem.</u> 196:151-155 (1991)		
___ DY	Smirnov, Y.V. et al., "Synthesis in <i>Escherichia coli</i> and a Rapid Method of Isolating High-Activity Recombinant His <sub>6</sub> DNA Polymerase from <i>Thermus aquaticus</i> ," <u>Russian J. Bioorganic Chem.</u> 21(5):341-342 (1995)		
___ DZ	Smith, L.M., "Sequence from spectrometry: A realistic prospect," <u>Nature Biotechnology</u> 14:1084-1087 (1996)		
___ EA	Smith, R.A.G. et al., "Chemical derivatization of therapeutic proteins," <u>TIBTECH</u> 11:397-403 (1993)		
___ EB	Solar, I. et al., "Linker modification introduces useful molecular instability in a single chain antibody," <u>Protein Engineering</u> 8(7):717-723 (1995)		
___ EC	Song, Z.H. et al., "Molecular Cloning and Chromosomal Localization of Human Genes Encoding Three Closely Related G Protein-Coupled Receptors," <u>Genomics</u> 28:347-349 (1995)		
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___ EI	Stemmer, W.P.C., "Searching Sequence Space, Using recombination to search more efficiently and thoroughly instead of making bigger combinatorial libraries," <u>Biotechnology</u> 13:549-553 (1995)		
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___ EL	Strader, C.D. et al., "The family of G-protein-coupled receptors," <u>FASEB J.</u> 9:745-754 (1995)		
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LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		Applicant: PHILLIP A. PATTEN et al. <del>unassigned</del>	
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— EO	Su, S.S. et al., "Escherichia coli mutS-encoded protein binds to mismatched DNA base pairs," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 83:5057-5061 (1986)
— EP	Suzuki, M. et al., "Random mutagenesis of <i>Thermus aquaticus</i> DNA polymerase I: Concordance of immutable sites in vivo with the crystal structure," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 93:9670-9675 (1996)
— EQ	Tabor S. et al., "DNA Sequence Analysis with a Modified Bacteriophage T7 DNA polymerase," <u>J. Biol. Chem.</u> 265(14):8322-8328 (1990)
— ER	Théze, J. et al., "Interleukin 2 and its receptors: recent advances and new immunological functions," <u>Immunol. Today</u> 17(10):481-486 (1996)
— ES	Turner, S.L. et al., "Use of Deoxyinosine in PCR to Improve Amplification of GC-Rich DNA," <u>Biotechniques</u> 19(1):48-52 (1995)
— ET	von der Osten, C. et al., "Protein engineering of subtilisins to improve stability in detergent formulations," <u>J. Biotech.</u> 28:55-68 (1993)
— EU	Wagner, R. et al., "Mutation detection using immobilized mismatch binding protein (MutS)," <u>Nucl. Acids Res.</u> 23(19):3944-3948 (1995)
— EV	Wall, J.G. et al., "Effects of overexpressing folding modulators on the in vivo folding of heterologous proteins in <i>Escherichia coli</i> ," <u>Current Op. Biotech.</u> 6:507-516 (1995)
— EW	Weck, P.K. et al., "Comparison of the Antiviral Activities of Various Cloned Human Interferon- $\alpha$ Subtypes in Mammalian Cell Cultures," <u>J. Gen. Virol.</u> 57:233-237 (1981)
— EX	Wettstein, D.A., "Expression of a Class II Major Histocompatibility Complex (MHC) Heterodimer in a Lipid-linked Form with Enhanced Peptide/Soluble MHC Complex Formation at Low pH," <u>J. Exp. Med.</u> 174:219-228 (1991)
— EY	Young, N.M. et al., "Thermal stabilization of a single-chain Fv antibody fragment by introduction of a disulphide bond," <u>FEBS Letts.</u> 377:135-139 (1995)
— EZ	Zhang, T. et al., "Circular Permutation of T4 Lysozyme," <u>Biochemistry</u> 32:12311-12318 (1993)
— FA	Zhao, X., "EPD, a novel technology for drug delivery," <u>Adv. Drug Deliv. Rev.</u> 17:257-262 (1995)
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EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 (Modified)

Attorney Docket No.

Serial No.:

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STATEMENT

(Use several sheets if necessary)

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Group: Unknown

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## Reference Designation

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Examiner Initial	Document No.	Date	Name	Class	Sub-class	Filing Date (If Appropriate)
AA	5,525,486	06/11/96	Honjo et al.	C12N	15/00	
AB	5,565,332	10/15/96	Hoogenboom et al.	435	69.1	
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AG	Crameri et al., "CONSTRUCTION AND EVOLUTION OF ANTIBODY-PHAGE LIBRARIES BY DNA SHUFFLING" Nature Medicine 2(1):100-102 (1996)
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AJ	O'Neil et al., "PHAGE DISPLAY: PROTEIN ENGINEERING BY DIRECTED EVOLUTION" Current Opinion in Structural Biology 5:443-449 (1995)
AK	Reikofski et al., "POLYMERASE CHAIN REACTION (PCR) TECHNIQUES FOR SITE-DIRECTED MUTAGENESIS" BIOTECH. ADV. 10:535-547 (1992)
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